Inflammation and prostate carcinogenesis
Influence of immune characteristics and early adulthood exposure to inflammatory conditions on prostate cancer risk

av

Henrik Ugge

Akademisk avhandling

Avhandling för medicine doktorsexamen i medicinsk vetenskap med inriktning mot kirurgi som kommer att försvaras offentligt fredag den 10 maj 2019 kl. 12.30, Hörsal C1, Campus USÖ, Örebro universitet

Opponent: docent Lars Henningsohn
Karolinska Institutet
Stockholm

Örebro universitet
Institutionen för Medicinska Vetenskaper
701 82 ÖREBRO
Abstract


Chronic inflammation has been implicated in the development of several types of cancer, and evidence from observational and animal studies suggests that it may play a role also in prostate carcinogenesis. Recent observations have brought *Cutibacterium acnes* (*C. acnes*) forward as a possible causative agent in pro-oncogenic prostatic inflammation. However, evidence also suggest that underlying immune characteristics contribute to prostate cancer risk. The overall aim of this thesis was to explore potential mechanisms underlying the proposed link between inflammation and prostate cancer, by evaluating associations between inflammatory conditions during early adulthood, circulating inflammation markers, and prostate cancer. Due to the suggested role of *C. acnes* in both diseases, we aimed to investigate whether acne vulgaris is a determinant of prostate cancer. Using prospectively collected data from Swedish national registers, we observed that presence of acne during early adulthood conferred an increased risk of prostate cancer later in life. Similarly, we found that appendicitis before late adolescence – a proposed marker of individual immune characteristics – to be positively associated with subsequent prostate cancer. We further evaluated whether prostatic *C. acnes* infection is linked with elevated systemic levels of IL6 and CXCL8, two inflammation markers previously associated with prostate cancer. No association was observed, however, potentially explained by the subclinical low-grade infection typically caused by *C. acnes*. Finally, we evaluated 52 circulating inflammation markers as determinants for prostate cancer in a population-based case-control study. In this hypothesis-generating study, we identified CX3CL1, CCL21, PDGF-BB, CCL11 and IL10 as candidate markers for evaluation in prospective studies. If confirmed, these markers may hint at targetable molecular pathways involved in prostate carcinogenesis.

*Keywords*: prostate cancer, inflammation, *Cutibacterium acnes*, acne, appendicitis, cytokines, circulating, inflammation marker, IL6, CXCL8.

Henrik Ugge, School of Medical Sciences
Örebro University, SE-701 82 Örebro, Sweden,
henrik.ugge@regionorebrolan.se